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LETTER TO THE EDITOR

Prolonged dyskinesia following lithium intoxication in an elderly patient with bipolar I disorder

Dear Editor,

A 67-year-old female patient with bipolar I disorder had been taking the medications lithium (900 mg daily) and quetiapine (600 mg daily) for 6 months. She unfortunately presented with confused consciousness, tremor of the four limbs, and diarrhea 3 days before visiting our emergency department. In the emergency department, the patient's body temperature was 38.9°C. The serum levels of lithium and creatinine were elevated at 3.18 mmol/L and 1.82 mg/dL, respectively. The patient's bilateral pupil size, blood pressure, electrocardiography, and oxygen saturation were normal. A lumbar puncture revealed normal results. Magnetic resonance imaging of the brain showed a symmetrical high signal intense lesion in the splenium of the corpus callosum on the three-direction diffusion image, which was consistent with axonal injury. There was no evidence of stroke, structural lesions, encephalitis, hepatic encephalopathy, blood sugar abnormality, and hypoxia of the brain, based on the magnetic resonance imaging evaluation. The fever subsided in 2 days. On the 3rd day after hospitalization, the levels of lithium (0.77 mmol/L) and creatinine (0.61 mg/dL) returned to within their normal ranges. The delirium unfortunately persisted and the patient developed involuntary movements such as biting and mouth chewing, and rapid, purposeless, irregular, and spontaneous choreic movements of her arms, wrists, and hands. Foot squirming and twisting of neck and shoulder were also noted. The involuntary movements subsided when sleeping.

We restored quetiapine monotherapy for her bipolar disorder. One month later, the delirium resolved and she could reply with simple words. However, the patient still had ataxia, dysarthria, and involuntary movement. Owing to severe involuntary movements, we added amantadine 50 mg twice daily; clonazepam, 0.5 mg twice daily; and haloperidol, 0.25 mg three times daily. Four weeks after prescribing medications (the baseline time point), the patient was able to try an oral diet. Six weeks after the baseline time point, the patient could sit on the bed for a few minutes.

Six months later, she had total recovery of the involuntary movements of the face, mouth, extremities, and trunk, but she still experienced the neurological sequelae of general weakness and dysarthria. Muscle power assessment revealed movement possible against gravity but without imposed resistance. As shown in Table 1, facial and oral involuntary movements showed early improvement 6 weeks later, and the improvement rate was lowest in Category IV of the Abnormal Involuntary Movement Scale (AIMS) [1], which encompasses the overall severity, the patient's awareness of the movements, and the distress associated with them.

Multiple etiologies may account for the development of chronic dyskinesia such as antipsychotics, encephalitis, a stroke involving the brainstem, nonketotic hyperglycemia, hepatocerebral degeneration, and hypoxic encephalopathy. In our patient, the aforementioned causes were excluded by the clinical evaluation.

Second-generation antipsychotics are reportedly less likely to induce extrapyramidal syndrome [2]. Therefore, we restored quetiapine therapy for maintenance treatment. The involuntary movement continued to improve during the period she used quetiapine. Quetiapine-induced involuntary movement was unlikely. Therefore, we believe that the patient's dyskinesia was related to lithium intoxication. Lithium treatment could reduce glutamate excitotoxicity in neurons and reveal a neuroprotective effect [3]. By contrast, at a toxic level, lithium may inhibit glutamate metabolism and allow excitotoxicity effects in the neurons in the striatum and cortex [4].

Conflicts of interest: The author declares no conflicts of interest.

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Table 1 Abnormal Involuntary Movement Scale scores and improvement in a patient with lithium intoxication.

	Baseline[a]	Baseline + 6 wks	Baseline + 12 wks	Baseline + 24 wks
Medications	Amantadine (100 mg daily), clonazepam (1.0 mg daily), haloperidol (0.75 mg daily)	The same as at baseline	The same as at baseline	Amantadine (100 mg daily), clonazepam (0.5 mg daily)
AIMS (categories I to III)				
I. Facial and oral movement	13	6 (53.8%)	5 (61.5%)	0 (100%)
II. Extremity movements	7	5 (28.6%)	4 (42.9%)	0 (100%)
III. Trunk movements	3	2 (33.3%)	1 (66.7%)	0 (100%)
Total score of I to III	23	13 (43.5%)	10 (56.5%)	0 (100%)
Global judgment[b]	12	9 (25%)	7 (41.7%)	4 (66.7%)

AIMS = Abnormal Involuntary Movement Scale.
The data are presented as the number or as the number (% improvement rate in the scores).
[a] The baseline is at 4 weeks after admission. We began to prescribe medications for dyskinesia.
[b] Category IV of the AIMS scale encompasses the overall severity, the patient's awareness of the movements, and the distress associated with the movements.

Glutamate excitotoxicity may increase cell ion permeability and lead to intracellular calcium overload, which is crucial for secondary axonal injury. Axonal injury may be caused by primary axotomy from mechanical forces and from secondary axotomy due to a series of biochemical events [5]. In our patient, although there was no evidence of trauma, a head injury may have occurred when her conscious was disturbed. However, based on the clinical findings, axonal injury in the patient can still be explained by lithium poisoning (i.e., a secondary cause) rather than by the primary causes of axonal injury. This injury indicates the consequences of decreased brain-derived neurotrophic factor axonal transport, diminished neurotrophic support of the striatum and cortex cells, and autophagy deficits by impaired axonal transport of autophagosomes. Moreover, a lower dose of lithium inhibits inositol monophosphatase, which induces autophagy; however, a higher dose inhibits glycogen synthase kinase-3β, which suppresses autophagy. Therefore, acute lithium intoxication in our patient could promote inositol monophosphatase activity and inhibit glycogen synthase kinase-3β to suppress autophagy [3]. We suggest that an older age may also explain the prolonged involuntary movement complication in this patient [2].

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